

**Amendments to the Claims:**

*This listing of the claims below will replace all prior versions and listing of claims in this application.*

Claims 1-1410 (Canceled)

Claim 1411 (Previously presented) A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (A) providing a sample which may contain a nucleic acid of interest;
- (B) providing:

- (i) an oligo- or polynucleotide that comprises two segments, the first segment comprising a nucleotide sequence that is complementary to and capable of specifically hybridizing to and forming a hybrid with said nucleic acid of interest or a portion thereof, and the second segment comprising an operator sequence that is capable of binding to or complexing with a non-radioactively detectable protein; and

- (ii) a non-radioactively detectable protein which is non-radioactive and has a binding affinity to said operator sequence;

- (C) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said non-radioactively detectable protein (ii) to form a complex; and

- (D) detecting non-radioactively the presence of said non-radioactively detectable protein in said complex to detect said nucleic acid of interest.

Claim 1412 (Previously presented) The process according to claim 1411, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

Claim 1413 (Previously presented) The process according to claim 1411, wherein the nucleic acid of interest is double-stranded or single-stranded.

Claim 1414 (Previously presented) The process according to claim 1411, wherein the nucleic acid of interest has been rendered single-stranded.

Claim 1415 (Previously presented) The process according to claim 1411, wherein the nucleic acid of interest is derived from an organism.

Claim 1416 (Previously presented) The process according to claim 1415, wherein the organism comprises prokaryotes or eukaryotes.

Claim 1417 (Previously presented) The process according to claim 1415, wherein said organism bacteria, fungi, viruses, yeast or mammals.

Claim 1418 (Previously presented) The process according to claim 1415, wherein said organism is living.

Claim 1419 (Previously presented) The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

Claim 1420 (Previously presented) The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent comprises bacteria, virus or fungi.

Claim 1421 (Previously presented) The process according to claim 1411, wherein said nucleic acid of interest is derived from an organism comprising *Streptococcus pyrogenes*, *Neisseria meningitides*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, or *Mycobacterium tuberculosis*.

Claim 1422 (Previously presented) The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae* sequences.

Claim 1423 (Previously presented) The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to

an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

Claim 1424 (Previously presented) The process according to claim 1423, wherein when said bacterium is *Streptococcus pyogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside.

Claim 1425 (Previously presented) The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic comprises penicillin, tetracycline, aminoglycoside or combinations thereof.

Claim 1426 (Previously presented) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

Claim 1427 (Previously presented) The process according to claim 1411, wherein said sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

Claim 1428 (Previously presented) The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes.

Claim 1429 (Previously presented) The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

Claim 1430 (Previously presented) The process according to claim 1411, wherein said non-radioactive detectable protein comprises an antibody, a promoter, a repressor or an inducer.

Claim 1431 (Previously presented) The process according to claim 1430, wherein said repressor comprises a lac repressor.

Claim 1432 (Previously presented) The process according to claim 1430, wherein said operator sequence is covalently attached to said oligo- or polynucleotide.

Claim 1433 (Previously presented) The process according to claim 1432, wherein said covalent attachment has been carried out by ligation.

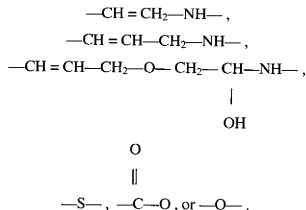
Claim 1434 (Previously presented) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to bind to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Claim 1435 (Previously presented) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to be detected non-radioactively when bound to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Claim 1436 (Previously presented) The process according to claim 1432, wherein said operator sequence is attached via a covalent attachment by an olefinic bond at the  $\alpha$ -position relative to the point of attachment to said nucleotide structure or nucleotide analog structure (i) , a  $\text{CH}_2\text{NH}$ — moiety, or both.

Claim 1437 (Previously presented) The process according to claim 1436, wherein said covalent attachment comprises an allylamine group.

Claim 1438 (Previously presented) The process according to claim 1436, wherein said covalent attachment comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties



Claim 1439 (Previously presented) The process according to claim 1432, wherein said covalent attachment comprises a glycosidic linkage moiety.

Claim 1440 (Previously presented) The process according to claim 1432, wherein said operator sequence is covalently attached to any of the base, phosphate, or furanosyl moieties in said oligo- or polynucleotide.

Claim 1441 (Previously presented) The process according to claim 1440, wherein said covalent attachment is through a linkage group.

Claim 1442 (Previously presented) The process according to claim 1441, wherein said linkage group comprises an amine.

Claim 1443 (Previously presented) The process according to claim 1442, wherein said amine comprises a primary amine.

Claim 1444 (Previously presented) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said operator sequence.

Claim 1445 (Previously presented) The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signalling component or indicator molecule.

Claim 1446 (Previously presented) The process according to claim 1445, wherein said signalling component or indicator molecule comprises at least three carbon atoms.

Claim 1447 (Previously presented) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1448 (Previously presented) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms.

Claim 1449 (Previously presented) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1450 (Previously presented) The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1451 (Previously presented) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1452 (Previously presented) The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1453 (Previously presented) The process according to claim 1446, wherein said signalling component or indicator molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1454 (Previously presented) The process according to claim 1445, wherein said signalling component or indicator molecule comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component a chelating component, or any combination of any of the foregoing.

Claim 1455 (Previously presented) The process according to claim 1445, wherein said signalling component or indicator molecule comprises an aromatic structure.

Claim 1456 (Previously presented) The process according to claim 1455, wherein said aromatic structure is heterocyclic.

Claim 1457 (Previously presented) The process according to claim 1456, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1458 (Previously presented) The process according to claim 1457, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl or any combination of any of the foregoing.

Claim 1459 (Previously presented) The process according to claim 1458, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1460 (Previously presented) The process according to claim 1454, wherein said signalling component or indicator molecule comprises a chemiluminescent component.

Claim 1461 (Previously presented) The process according to claim 1454, wherein said signalling component or indicator molecule comprises a chelating component.

Claim 1462 (Previously presented) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1463 (Previously presented) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest.

Claim 1464 (Previously presented) The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide directly or through a linkage group.

Claim 1465 (Previously presented) The process according to claim 1411, wherein said oligo- or polynucleotide is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein.

Claim 1466 (Previously presented) The process according to claim 1411, wherein said detecting step is carried out directly.

Claim 1467 (Previously presented) The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signalling components or indicator molecules.

Claim 1468 (Previously presented) The process according to claim 1467, wherein said direct detection step is carried out by a fluorogenic structure, a chemiluminescent structure, an enzyme, or an electron dense structure.



Claim 1469 (Previously presented) The process according to claim 1411, wherein said detecting step is carried out indirectly.

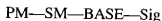
Claim 1470 (Previously presented) The process according to claim 1469, wherein said indirect detection is carried out by a means comprising an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a structure capable of binding to an insoluble phase, or a combination of any of the foregoing.

Claim 1471 (Previously presented) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1472 (Previously presented) The process according to claim 1411, further comprising one or more washing steps.

Claim 1473 (Previously presented) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising: providing at least one cell; contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

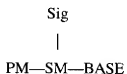
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

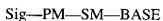
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,  
SM is a furanosyl moiety,  
BASE is a base moiety, and  
Sig is a detectable non-radioactive moiety,

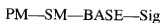
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1474 (Previously presented) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising: providing at least one cell; providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

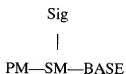
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

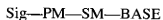
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,  
BASE is a base moiety, and  
Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides,

permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

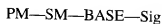
detecting non-radioactively any of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

Claim 1475 (Previously presented) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising: providing at least one cell; providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein said clones or fragments or said oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator moiety and each of said clones or DNA fragments or oligo- or polynucleotides comprises one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or

coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

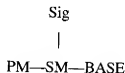
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

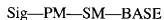
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group ;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting non-radioactively any of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

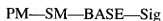
Claim 1476 (Previously presented) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

providing at least one interphase cell;

providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones, wherein said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest and each of said clones or DNA fragments or oligo- or

polynucleotides in said sets comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more of :

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

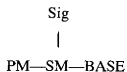
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,



BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and  
Sig is a detectable non-radioactive moiety,  
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,  
SM is a furanosyl moiety,  
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and  
Sig is a detectable non-radioactive moiety,  
wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides,

permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and

comparing each generated signal with other generated signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Claim 1477 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1478 (Previously presented) The process according to claim 1477, wherein said enzyme comprises terminal transferase.

Claim 1479 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog has been coupled to DNA or RNA by a coupling means comprising chemical coupling or enzymatic coupling.

Claim 1480 (Previously presented) The process according to claim 1479, wherein said chemical coupling has been carried out by a chemical coupling means comprising carbodiimide or formaldehyde.

Claim 1481 (Previously presented) The process according to claim 1479, wherein said enzymatic coupling has been carried out by an enzymatic coupling means comprising DNA ligase or RNA ligase.

Claim 1482 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation.

Claim 1483 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1484 (Previously presented) The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase.

Claim 1485 (Previously presented) The process according to claim 1484, wherein said polymerase comprises DNA polymerase or RNA polymerase.

Claim 1486 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetraphosphate.

Claim 1487 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises nucleoside mono-, di- or tri-phosphate.

Claim 1488 (Canceled)

Claim 1489 (Canceled)

Claim 1490 (Previously presented) The process according to claim 1473, 1474, 1475 or 1476, wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'-dideoxyribose.

Claim 1491 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein BASE in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a 7-deazapurine.

Claim 1492 (Canceled)

Claim 1493 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (i) is covalently attached to BASE the C2 position, the N3 position, the C6 position, or combinations thereof when BASE is a pyrimidine, or is covalently attached to BASE the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof when BASE is a purine.

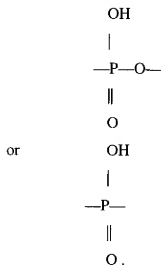
Claim 1494 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (i) is covalently attached to BASE at a position comprising the N<sup>4</sup> position when said pyrimidine comprises cytosine, the N<sup>2</sup> position when said purine comprises adenine or deazaadenine, the N<sup>6</sup> position when said purine comprises guanine or deazaguanine, or combinations thereof.

Claim 1495 (Previously presented) The process according to claim 1473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from

the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1496 (Previously presented) The process according to claim 1473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (iii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1497 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog structure (iii) comprises



Claim 1498 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1499 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claim 1500-1503 (Canceled)

Claim 1504 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1505 (Previously presented) The process according to claim 1504, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group contains an amine.

Claim 1506 (Previously presented) The process according to claim 1505, wherein said amine comprises a primary amine.

Claim 1507 (Previously presented) The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1508 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms.

Claim 1509 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1510 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

Claim 1511 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1512 (Previously presented) The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1513 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1514 (Previously presented) The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1515 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1516 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component, or any combination of any of the foregoing.

Claim 1517 (Canceled)

Claim 1518 (Previously presented) The process according to claim 1516, wherein said electron dense component comprises ferritin.

Claim 1519 (Canceled)

Claim 1520 (Previously presented) The process according to claim 1516, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 1521 (Previously presented) The process according to claim 1516, wherein said magnetic component comprises magnetic beads.

Claim 1522 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

Claim 1523 (Previously presented) The process according to claim 1522, wherein the binding protein comprises a lectin.

Claim 1524 (Previously presented) The process according to claim 1523, wherein the lectin comprises concanavalin A.

Claim 1525 (Previously presented) The process according to claim 1523, wherein said lectin is conjugated to ferritin.

Claim 1526 (Canceled)

Claim 1527 (Previously presented) The process according to claim 1516, wherein said enzyme comprises alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

Claim 1528 (Canceled)

Claim 1529 (Canceled)

Claim 1530 (Previously presented) The process according to claim 1516, wherein said metal-containing component is catalytic.

Claim 1531 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is a non-radioactively detectable indicator molecule.

Claim 1532 (Previously presented) The process according to claim 1531, wherein said indicator molecule comprises an aromatic structure.

Claim 1533 (Previously presented) The process according to claim 1532, wherein said aromatic structure is heterocyclic.

Claim 1534 (Previously presented) The process according to claim 1533, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1535 (Previously presented) The process according to claim 1534, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Claim 1536 (Previously presented) The process according to claim 1535, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1537 (Previously presented) The process according to claim 1516, wherein Sig comprises a fluorescent component.

Claim 1538 (Previously presented) The process according to claim 1516, wherein said fluorescent component comprises fluorescein, rhodamine or dansyl.

Claim 1539 (Previously presented) The process according to claim 1538, wherein said fluorescent component comprises fluorescein.

Claim 1540 (Canceled)



Claim 1541 (Previously presented) The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

Claim 1542 (Canceled)

Claim 1543 (Canceled)

Claim 1544 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is a non-radioactively detectable indicator molecule.

Claim 1545 (Previously presented) The process according to claim 1544, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

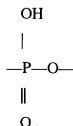
Claim 1546 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) and (iii) are detectable by a means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1547 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

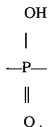
Claim 1548 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group.

Claim 1549 (Previously presented) The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Claim 1550 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (iii) is covalently attached to PM via the chemical linkage



Claim 1551 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (iii) is covalently attached to PM via a chemical linkage.



Claim 1552 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

Claim 1553 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

Claim 1554 (Previously presented) The process according to claim 1552, wherein the polypeptide comprises a polylysine.

Claim 1555 (Previously presented) The process according to claim 1553, wherein the polypeptide comprises a polylysine.

Claim 1556 (Previously presented) The process according to claim 1552, wherein the polypeptide comprises avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1557 (Previously presented) The process according to claim 1553, wherein the polypeptide comprises avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1558 (Previously presented) The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1559 (Previously presented) The process according to claim 1553, wherein the moiety which can be detected when the complex is formed comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component, or any combination of any of the foregoing.

Claim 1560 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly.

Claim 1561 (Previously presented) The process according to claim 1560, wherein said direct detection is carried out on one or more non-radioactively detectable indicator molecules.

Claim 1562 (Previously presented) The process according to claim 1561, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 1563 (Previously presented) The process according to claim 1562, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1564 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety.

Claim 1565 (Previously presented) The process according to claim 1564, wherein said detecting step is carried out by a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 1566 (Previously presented) The process according to claim 1564, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

Claim 1567 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said Sig detectable non-radioactive moiety.

Claim 1568 (Previously presented) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 1569 (Canceled)

Claim 1570 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1571 (Previously presented) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps.

Claim 1572 (Previously presented) The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

Claim 1573 (Previously presented) The process according to claim 1475, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

Claim 1574 (Previously presented) The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means comprising manual means or automatic means.

Claim 1575 (Previously presented) The process according to claim 1574, wherein said manual means comprises visualization.

Claim 1576 (Previously presented) The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping.

Claim 1577 (Previously presented) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

Claim 1578 (Previously presented) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule.

Claim 1579 (Previously presented) The process according to claim 1476, wherein said detecting and determining step is carried out by a means comprising manual means or automatic means.

Claim 1580 (Previously presented) The process according to claim 1579, wherein said manual means comprises visualization.

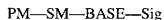
Claim 1581 (Previously presented) The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping.

Claim 1582-1704 (Canceled)

Claim 1705 (Previously presented) A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (a) providing a sample which may comprise a nucleic acid of interest;
- (b) providing a metal or metal ion;
- (c) specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

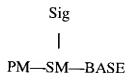
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a signalling moiety comprising a chelating structure or component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

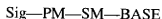
PM is a phosphate moiety ,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or component capable of providing chelating said metal or metal ion and a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety ,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or components capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2', 3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(d) detecting the presence of Sig in any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest by means of said metal or metal ion chelated by said chelating structure or chelating components.

Claim 1706 (Previously presented) A process for detecting a nucleic acid of interest in a sample, which process comprises:

(A) providing:

(i) an oligo- or polynucleotide having two segments:

(a) a first segment complementary to and capable of hybridizing to a portion of said nucleic acid of interest; and

(b) a second segment comprising at least one protein binding sequence; and

(ii) a metal or metal ion;

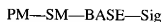


- (iii) a detectable protein capable of binding to said protein binding sequence and comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal;
- (B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide and said detectable protein (ii) to form a complex;
- (C) detecting the presence of said protein in said complex and said nucleic acid of interest by means of said metal or metal ion chelated by said chelating structure or chelating component.

Claim 1707 (Previously presented) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising:

- providing a cell;
- providing a metal or metal ion;
- contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

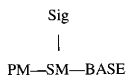
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

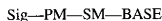
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides by means of said metal or metal ion chelated by said chelating structure or chelating component, and determining the number of copies of said particular chromosome;

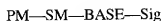
comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome; and

determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1708 (Previously presented) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising:

- providing a cell;
- providing a metal or metal ion;
- providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

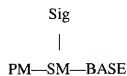
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

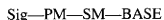
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

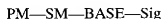
Claim 1709 (Previously presented) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising:

providing a cell of interest;

providing a metal or metal ion;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA and wherein each set comprises a different indicator molecule, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

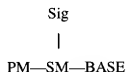
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

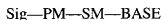
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the

locus or loci in said chromosomes, and identifying a plurality or all of the chromosomes in said cell of interest.

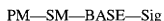
Claim 1710 (Previously presented) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

providing an interphase cell of interest;

providing a metal or metal ion;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analog comprise a nucleotide structure or nucleotide analog structure comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

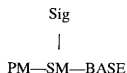
BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the



C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

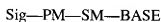
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes; and

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Claim 1711 (Previously presented) A process for preparing a labeled oligo- or polynucleotide of interest, comprising:

(A) providing a metal or metal ion;

(B) providing:

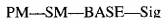
(1) one or more detectable chemically modified or labeled nucleotides or detectable chemically modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more signalling moieties comprising a chelating structure or chelating component capable of chelating a metal or metal ion and providing a detectable signal,

(2) an oligo- or polynucleotide comprising one or more of said modified or labeled nucleotides or modified or labeled nucleotide analogs (1), alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, or

(3) both (1) and (2).

wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs (1) are modified on the furanosyl moiety, the phosphate moiety, the base moiety or any combination thereof, and wherein the modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising :

(i)



wherein

PM is a phosphate moiety,

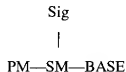
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii)



wherein

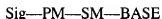
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a signal, wherein Sig comprises at least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii)



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal; wherein Sig comprises at least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and said oligo- or polynucleotide of interest; and (C) either incorporating said modified or labeled nucleotides or modified or labeled nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

Claim 1712 (Previously presented) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing a sample which may contain a nucleic acid of interest;

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotides or polynucleotides, each of said detectable non-radioactively labeled oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest;

forming in liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest;

separating or resolving in a gel said formed hybrids; and  
detecting non-radioactively the separated or resolved hybrids to detect the presence of said nucleic acid of interest.

Claim 1713 (Previously presented) The process according to claim 1712, further comprising after said hybrid forming step, the step of subjecting the liquid phase to nuclease treatment.

Claim 1714 (Previously presented) The process according to claim 1712, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1715 (Previously presented) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprises DNA, RNA or DNA-RNA.

Claim 1716 (Previously presented) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or a combination of any of the foregoing.

Claim 1717 (Previously presented) The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly.

Claim 1718 (Previously presented) The process according to claim 1712, wherein said detecting step is carried out by means of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1719-1726 (Canceled)

Claim 1727 (Previously presented) The process according to claim 1712, wherein said detecting step comprises localizing said separated or resolved hybrids.

Claim 1728-1729 (Canceled)

Claim 1730 (Previously presented) The process of claim 1705, wherein in said specific hybridizing step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1731 (Previously presented) The process of claim 1707, wherein in said contacting step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1732-1748 (Canceled)

Claim 1749 (Previously presented) The process of any of claims 1706, 1708, 1709, 1710 or 1711, wherein in said providing step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1750 (Previously presented) The process of any of claims 1705, 1706, 1707, 1708, 1709 or 1710, wherein said detecting step is carried out by a structure or component that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1751 (Previously presented) The process of any of claims 1705, 1706, 1707, 1708, 1709, or 1710, wherein in said detecting step, the chelating structure or chelating components have a chelated metal or metal ion comprising heavy metals or rare earth metals.

Claim 1752 (Previously presented) The process of claim 1751, wherein said heavy metal comprises cobalt.

Claim 1753 (Previously presented) The process of claim 1750, wherein said detecting step is carried out radioactively.

Claim 1754 (Previously presented) The process of claim 1753, wherein said radioactive detection is carried out by means of an isotope.

Claim 1755 (Previously presented) The process of claim 1754, wherein said isotope is a  $\beta$  or  $\gamma$  emitter.

Claim 1756 (Previously presented) The process of claim 1753, wherein said radioactive detection is carried out with an isotope comprising bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 or yttrium-90.

Claim 1757 (Previously presented) The process of any of claims 1450, 1452, 1512, or 1514, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

Claim 1758-1759 (Canceled)

Claim 1760 (Previously presented) The process of any of claims 1473, 1474, 1475, 1476, 1705, 1707, 1708, 1709, 1710, or 1711, wherein said base comprises a pyrimidine analog or a purine analog.

Claim 1761 (Previously presented) The process of claim 1760, wherein said pyrimidine analogs comprise thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs or deoxycytidine analogs.

Claim 1762 (Previously presented) The process of claim 1761, wherein said uridine analogs comprise 5-bromo-2'-deoxyuridine-5'-phosphate.

Claim 1763 (Previously presented) The process of claim 1761, wherein said deoxycytidine analogs comprise 5-hydroxymethyl-2'-deoxycytidylic acid.

Claim 1764 (Previously presented) The process of claim 1760, wherein said purine analog comprises adenosine analogs, deoxyadenosine analogs, guanosine analogs or deoxyguanosine analogs.

Claim 1765 (Previously presented) The process of claim 1764, wherein said adenosine analogs comprise tubericidin or toyocamycin.

Claim 1766-1783 (Canceled)

Claim 1784 (Previously presented) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotide or polynucleotide, each of said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to, coupled to, or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest;

forming liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest; subjecting said liquid phase to nuclease treatment to digest non-hybridized single-stranded detectable non-radioactively labeled oligonucleotides or polynucleotides and leave said hybrids intact; and

detecting the hybrids non-radioactively to detect the presence of said nucleic acid of interest.

Claim 1785 (Currently amended) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) a detectable non-radioactively labeled oligonucleotide or polynucleotide, said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotide or polynucleotide comprises one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which



nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest; and

forming in liquid phase, hybrids comprising said detectable non-radioactively labeled oligonucleotide or polynucleotide specifically hybridized with said nucleic acid of interest; and  
detecting hybrids non-radioactively to detect the presence of said nucleic acid of interest.

Claim 1786 (Previously presented) The process according to claim 1785, further comprising a treatment that acts upon a non-hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide and leaves a hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide intact.

Claim 1787 (Previously presented) The process according to claim 1786 wherein said treatment is a nuclease treatment.

Claim 1788 (Previously presented) The process according to claim 1784 or 1787 wherein said nuclease treatment is carried out by S1 nuclease, Exonuclease I from *E.coli*, or a combination thereof.

Claim 1789 (Previously presented) The process according to any of claims 1784, 1785, 1786 or 1787 further comprising separating or resolving in a gel said formed hybrids.

Claim 1790 (Previously presented) The process according to claim 1784 or 1785, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1791 (Previously presented) The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises DNA, RNA or DNA-RNA.

Claim 1792 (Previously presented) The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing

component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or a combination of any of the foregoing.

Claim 1793 (Previously presented) The process according to claim 1784 or 1785, wherein said non-radioactive detection step is carried out directly or indirectly.

Claim 1794 (Previously presented) The process according to claim 1784 or 1785, wherein said detecting step is carried out by means of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1795 (Canceled)